protein, have shown activity by inducing an active immune response against tumor cells. Randomized studies have shown that using the ipilimumab antibody allows a significant increase in survival compared to standard chemotherapy in patients with advanced metastatic melanoma.

[0008] The most commonly used chemotherapy regimens in the treatment of tumors of the gastrointestinal tract are usually combinations of multiple drugs to allow extension of overall survival. Said regimens substantially provide the use of antimetabolite chemotherapeutics (e.g. 5-fluorouracil and derivatives thereof or gemcitabine) in association with camptothecins (e.g. Irinotecan) or platinum compounds (e.g. oxaliplatin). Anti-EGFR monoclonal antibodies or anti-angiogenic drugs, such as for example bevacizumab, ramucirumab and regorafenib, are also used.

[0009] With regard to thyroid carcinoma therapy, ablation of the thyroid residue by iodine-131 is generally recommended following thyroidectomy. The purpose of the radiometabolic therapy with iodine 131 is to destroy the normal thyroid tissue, which almost always remains even after total thyroidectomy, and eliminate any neoplastic microfoci inside the thyroid residues or in other sites. Finally, radiation therapy, chemotherapy and tyrosine kinase inhibitors are recommended in the case of highly aggressive and inoperable tumors or those characterized by de-differentiation, although with extremely limited efficacy results.

[0010] Melanocortins are peptide hormones derived from proteolytic cleavage of proopiomelanocortin (POMC) and include α-, β-, γ-MSH (melanocyte stimulating hormone) and adrenocorticotropin (ACTH). These hormones are present in serum and many tissues, such as the central nervous system (CNS) and the skin, and have a wide range of effects mediated by five different G protein-coupled transmembrane receptor subtypes. Receptor 1 (MC1R) is mainly expressed in melanocytes and mediates the effects on skin and hair pigmentation, whereas receptor 2 (MC2R) is mainly expressed in the adrenal cortex, where it mediates the effects of ACTH on glucocorticoid synthesis and release. The main sites of expression of receptor 5 (MC5R) are the exocrine glands and skeletal muscle. As for the expression of receptors 3 and 4 (MC3R, MC4R), it is mainly, but not exclusively, located in the central nervous system. In particular, the MC4R receptor is widely distributed in the brain areas of the hypothalamus, thalamus and cortex, with a particularly high concentration in the paraventricular nucleus and the lateral hypothalamic area, which are regions that play a key role in regulating the energy balance. Indeed, studies conducted on murine models have shown that MC4R receptors are involved in feeding behaviour, metabolism regulation, sexual behaviour, and male erectile function.

[0011] MC4R gene mutations have been reported as associated with human hereditary obesity, with a prevalence of 1.0-2.5% in individuals with body mass indexes above 30, thus making it the most common, known genetic defect predisposing to obesity. Pharmacological modulation of the activity of this receptor therefore represents a therapeutic approach of great interest in the field of metabolic diseases. In particular, a small molecule that acts as a selective non-peptide antagonist of MC4R has been synthesized and used experimentally to counteract the weight loss that occurs in patients suffering from sarcopenia and neoplastic cachexia (Vos T J et al.; Identification of 2-[2-[2-(5-bromo-2-methoxyphenyl)-ethyl]-3-fluorophenyl]-4,5-dihydro-1H-imidazole, a small molecule melanocortin 4 receptor antagonist that effectively reduces tumor-induced weight loss in a mouse model. J Med Chem. 2004; 47: 1602-1604). Recent studies have also shown that MC4R stimulation with agonists causes a major cytoprotective action in different tissues under hypoxic conditions, such as myocardial ischemia, stroke, head injury and haemorrhagic shock, as well as the ability of inducing neurogenesis (development of new functioning neurons), by stimulating cell proliferation activity. The scientific paper by Vaglini F et al. (Melanocortin Receptor-4 and Glioblastoma Cells: Effects of the Selective Antagonist ML00253764 Alone and in Combination with Temozolomide In Vitro and In Vivo. Mol Neurobiol. 2018; 55: 4984-4997) described for the first time the presence of the functionally active MC4R receptor in glioblastoma tumor cells, as well as the anti-tumor effect in this particular cell type mediated by the inhibition of this receptor through the use of selective antagonists.

[0012] Patent application US 2002/0004485 describes the action of peptide antagonists of melanocortin receptors on pigmentation in melanophores of *Xenopus laevis* larvae and in mammalian cells stably transfected with DNA encoding the aforementioned receptors. This patent application mentions the use of melanocortin antagonists for the therapeutic treatment of melanoma in a totally speculative manner. However, no support or experimental evidence is provided in this regard.

[0013] In this context, therefore, the dramatic need arises for the development of therapeutic strategies aimed at eradicating aggressive tumor diseases such as melanoma, tumors of the gastrointestinal tract and thyroid carcinoma, by contrasting their onset and progression, which are suitable for obtaining a lasting clinical response as well as preventing tumor recurrence.

[0014] Therefore, the object of the present invention is to provide a medicament capable of contrasting with high efficacy the growth and proliferation of melanoma, tumors of the gastrointestinal tract and thyroid carcinoma, while reducing possible adverse effects to a minimum extent.

[0015] Another object is to provide a medicament which is active as an adjuvant in cancer therapeutic treatment and at the same time effective in preventing and inhibiting the onset of metastases of these neoplasms.

[0016] A further object is to provide a medicament which, in addition to the aforementioned anti-tumor activity, is effective in controlling the neoplastic cachexia pathological condition typically associated with the advanced stages of melanoma, tumors of the gastrointestinal tract and thyroid carcinoma.

[0017] These and other objects are achieved by means of a melanocortin receptor-4 antagonist for use in the therapeutic treatment of a tumor pathology selected from the group consisting of melanoma, tumors of the gastrointestinal tract and thyroid carcinoma, as defined in the appended claim **1**.

[0018] Preferred embodiments of the invention form the subject of the remaining dependent and independent claims.

[0019] The appended independent and dependent claims form an integral part of the present specification.

[0020] As will be explained in more detail in the following experimental section, the present inventors have shown for the first time the presence of the melanocortin receptor 4 (MC4R) and its functional activity in cells isolated from some types of human solid tumors, more particularly in cells isolated from melanoma, tumors of the gastrointestinal tract